DOWNLOAD PDF METABOLISM BIOLOGICAL ACTIVITIES OF C(2)-CERAMIDE

Chapter 1 : metabolism | Definition, Process, & Biology | www.nxgvision.com

To investigate the effects of hypoxia-inducible factor (HIF) inhibitors, flotation agents, barriers, and a surfactant on pneumoperitoneum-enhanced adhesions in a laparoscopic mouse model.

This is an open access article distributed under the Creative Commons Attribution License , which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. Abstract Baicalin is one of the major bioactive constituents of Scutellariae Radix, but the biotransformation of it is poorly understood. In this paper, the metabolism of baicalin in rat was studied. Nine metabolites including one new compound were isolated and identified structurally. The plausible scheme for the biotransformation pathways of baicalin in the rats was deduced. And the main metabolites were evaluated for their antioxidation and anti-inflammation biological activities for the first time. Introduction Scutellariae Radix, the root of Scutellariae baicalensis Georgi, is widely used in traditional Chinese formulations. Baicalin baicalein 7-O-glucuronide is one of the major bioactive constituents of it, which possesses antiallergic, anti-inflammatory activity and antioxidation and has been used for the treatment of hepatitis, hyperlipidemia, and lipolysis [1]. It is well known that the process of drug metabolism affects therapeutic effects of drug. The biotransformation of baicalin is poorly understood, and that is due in part to difficulties that have been encountered in obtaining enough amounts to identify the structure of the metabolites and study the bioactivities of them. Although some works on the metabolism of baicalin have been investigated with the development of chromatography-spectrographic technology, because of the lack of metabolites quantitatively, many questions about the biological activities of the metabolites still remained after administration [2 â€” 5]. To gain additional insight into its metabolism and the biological activities of the metabolites, we isolated the metabolites from urine and feces of rats and identified their structures on the basis of physicochemical properties and spectroscopic data analysis. Nine metabolites including one new compound were obtained. At the same time, the antioxidation and anti-inflammation biological activities of the metabolites were investigated. It is the first time that the metabolism and the bioactivities of the metabolites of baicalin were studied comprehensively. Materials and Methods 2. Drugs Baicalin was isolated and purified from Scutellariae Radix according to the method reported previously [6]. Dosing Procedure Seven-week old Wistar rats five males and five females , weighing to g, were used for the experiments. Feces samples from rats were combined, suspended in the water and adjusted to PH 7 with NaHCO3-saturated aqueous solution, and then filtrated. Identification of Baicalin and Metabolites 2. The plausible scheme for the biotransformation pathways of baicalin in the rats. Biological Activities of the Metabolites 2. Antioxidation Livers were obtained from rats and disposed of the blood. All the numbered tubes were added with 1. Negative control was physiological saline. All the tubes were mixed, and standing for 10 min, centrifuged at rpm for 10 min. The supernatant was added with 0. The cool solution was tested on spectrophotometer at nm to obtain data. The supernatant was discarded. The cells were incubated overnight. The culture medium was changed to serum-free medium. After 24 h of incubation, the contents of in medium were tested with Griess colorimetry. Experimental results were analyzed statistically with SPSS software. Results and Discussion 3. The Metabolism of Baicalin in Rats Baicalin was orally administered to rats. The collected urine and feces samples were extracted and analyzed as described in experimental part. The structures of metabolites were elucidated by a combination analysis of their chromatographic behavior, analysis of MS, 1HNMR data, NOESY data, and spectral comparison to several reference substances. So M1 and M5 were identified as baicalin and baicalein, respectively. All these showed that there were two glucuronides at the position of C-6 and C Metabolites M6, M7, and M8 Compared with the 1HNMR spectrum of baicalin, there was no glucuronide signal but one methyl proton in these three metabolites. Therefore, the chemical structure of M6 was determined as 7-O-methyl-baicalein. The chemical structure of M7 was determined as 6-O-methyl-baicalein compared with reference [7]. M8 had the different retention characteristic with M6 and M7. The chemical

shift of the proton at position 5 of the glucuronide shifted to downfield by 0. To our knowledge, this compound was the first time to be isolated and identified. Based on the structures of these metabolites, a plausible scheme for the biotransformation pathways of baicalin in the rats was shown in Figure 2. The results of the present study demonstrated that the major metabolites of baicalin were baicalin, baicalein, and glucuronide after oral administration, and at the same time, small amount of alkylated products were also found, which was a little different from [4]. This may be for the more alkylation reacted on glucuronides and aglycone with longer time. The baicalin is very difficult to be absorbed into blood directly [8]. Thus, baicalein can be easily absorbed into blood. Through enterohepatic circulation, baicalein was transformed to glucuronides and then modified to kinds of alkylated glucuronides to demonstrate bioactivities. The Biological Activities of the Metabolites The effects of baicalin M1 and the metabolites M5 , M2 on liver lipid peroxide of rats were studied as shown in Figure 3. Baicalein M5 was even much stronger. As described above, baicalin was metabolized to baicalein, glucuronide, and methylated products though metabolism of intestinal bacteria and enterohepatic circulation. Although studies on the metabolism of drugs have been investigated with the development of LC-MS, the bioactivities on metabolites are still lacking of investigation. The results of bioactive experiments of these metabolites in our experiments demonstrated that baicalein and glucuronide showed significant potential on antioxidation and affections on LPS-induced NO yielding compared with reference substance. However, when substituents were replaced by alkyl, bioactivity was depressed. To our knowledge, this is the first time that the metabolites of baicalin were investigated on the antioxidation and anti-inflammation biological activities. These results suggested though baicalein had good biological availability, it could not be used for its instability, while glucuronides of baicalein will be the perspective lead compounds for their good stability and bioactivities. Acknowledgments The authors thank Mr. Wenjun Pan of Shenyang Pharmaceutical University for his experimental assistance. View at Google Scholar Follow Us.

DOWNLOAD PDF METABOLISM BIOLOGICAL ACTIVITIES OF C(2)-CERAMIDE

Chapter 2 : Marine Omega-3 Phospholipids: Metabolism and Biological Activities

REVIEW Open Access Endocannabinoids and related N-acylethanolamines: biological activities and metabolism Kazuhito Tsuboi1,2, Toru Uyama1, Yasuo Okamoto2 and Natsuo Ueda1.*

Basic composition of a ceramide The initiation of the synthesis of the sphingoid bases sphingosine, dihydrosphingosine, and the various ceramides takes place via the condensation of palmitoyl-CoA and serine as shown in the Figure below. This reaction occurs on the cytoplasmic face of the endoplasmic reticulum ER and is catalyzed by the pyridoxal phosphate -dependent enzyme, serine palmitoyltransferase SPT. The product of this reaction is 3-ketosphinganine 3-ketodihydrosphingosine. SPT is the rate-limiting enzyme of the sphingolipid biosynthesis pathway. Active SPT is a heterodimeric enzyme composed of two main catalytic subunits. An additional protein associates with the catalytic subunits to greatly enhance the activity of the enzyme complex as well as to confer acyl-CoA preference to the complex. Following formation of 3-ketosphinganine this compound is reduced to sphinganine dihydrosphingosine via the action of 3-ketosphinganine reductase 3-ketodihydrosphingosine reductase. The 3-ketosphinganine reductase enzyme is encoded by the KDSR gene which is located on chromosome 18q Sphinganine is then fatty acylated generating dihydroceramide. The acylation of sphinganine also called dihydrosphingosine occurs through the activities of six different ceramide synthases CerS in humans. These CerS enzymes introduce fatty acids of varying lengths [designated by the â€" CH2 nâ€" in the structure] and degrees of unsaturation. In other organisms the ceramide synthases are referred to as sphinganine N-acyl transferases. The actions of CerS and the role of ceramide in biological responses is covered below. Dihydroceramide is then unsaturated in the original palmitic acid portion of the molecule by the enzyme dihydroceramide desaturase 1 DES1. The official designation for DES1 is delta 4 -desaturase, sphingolipid 1 which is encoded by the DEGS1 gene located on chromosome 1q Following conversion to ceramide, sphingosine is released via the action of ceramidase. Sphingosine can be re-converted to a ceramide by condensation with a fatty-acyl-CoA catalyzed by the various CerS enzymes. There are at least two ceramidase genes in humans, both of which are defined by their pH range of activity: When studied in mice it has been shown that the ASAH1 gene is critical for early embryo survival and for removing ceramide from the embryo to prevent the default apoptosis pathway. Neutral ceramidase non-lysosomal ceramidase is encoded by the ASAH2 gene and the enzyme is expressed in the apical membranes of the proximal and distal tubules of the kidney , endosome-like organelles in heptocytes, and in the epithelial cells of the gut. The ASAH2 gene is located on chromosome 10q By studying the effects of ASAH2 knock-out mice it has been determined that neutral ceramidase is involved in the catabolism of dietary sphingolipids and the regulation of bioactive sphingolipid metabolites in the intestinal tract. Pathway for ceramides and sphingosine synthesis. The synthesis of ceramides can occur via the de novo pathway or the hydrolysis pathway. The de novo pathway begins with the transamination of palmitoyl-CoA via a condensation reaction with serine. This reaction, catalyzed by serine palmitoyltransferase, represents the rate-limiting step in ceramide synthesis. The hydrolysis pathway not shown to ceramides utilizes sphingomyelins as the substrates through the action of sphingomyelinase. Ceramides can serve as the substrates for sphingosine synthesis and sphingosine can serve as a substrate for ceramide synthesis, as depicted, through the actions of ceramidases and ceramide synthases. Sphingomyelins are important structural lipid components of nerve cell membranes. The predominant sphingomyelins contain palmitic or stearic acid N-acylated at carbon 2 of sphingosine. Sphingomyelins represent a class of lipid and the N-acylated fatty acid can be of varying lengths as well as being unsaturated. The sphingomyelin depicted contains the carbon saturated fatty acid, stearic acid. The sphingomyelins are synthesized by the transfer of phosphorylcholine from phosphatidylcholine to a ceramide in a reaction catalyzed by sphingomyelin synthases SMS. Expression of the SGMS1 gene predominates in the brain. The SMS2 enzyme is encoded by the SGMS2 gene located on chromosome 4q25 which is composed of 11 exons that generate three alternatively spliced mRNAs, all of

which encode the same amino acid protein. Metabolism of the sphingomyelins. The interconversion of ceramides and sphoingomyelins occurs as a result of the actions of sphingomyelinases and sphingomyelin synthases. The fatty acid incorporated into a ceramide by sphingomyelin synthases is most commonly derived from a phosphatidylcholine, PC. As shown in the Figure above, sphingomyelins are degraded via the action of sphingomyelinases resulting in release of ceramides and phosphocholine. The sphingomyelinase in humans functions at acidic pH and is, therefore, referred to as acid sphingomyelinase ASMase or aSMase. The human ASMase is encoded for by the sphingomyelin phosphodiesterase-1 gene gene symbol: SMPD1 which is located on chromosome 11p There are in fact two major forms of Niemann-Pick NP disease. With respect to the sphingomyelins they serve a dual purpose of being important membrane phospholipids and as a reservoir for ceramides. The conversion of both dihydrosphingosine sphinganine and sphingosine to ceramide is catalyzed by the ceramide synthases CerS. CerS were originally referred to as Lass genes for Longevity Assurance based on their homology to the yeast gene, longevity assurance gene-1 LAG1. LAG1 was so-called because deletion of the gene in yeast prolonged their life-span. An additional related gene in yeast is referred to as LAC1 and when both genes are deleted yeast exhibit poor growth or die. A human gene, originally identified as UOG-1 upstream of growth and differentiation factor-1 , was shown to complement a LAG1 deletion in yeast and when overexpressed in mammalian cells resulted in increased ceramide synthesis. The ceramides synthesized by the enzyme contained exclusively stearic acid C18 saturated fatty acid. Subsequent studies demonstrated that other human LAG homologs, originally identified as translocating chain-associating membrane proteins TRH synthesized ceramides with varying fatty acyl chain length. Each of these genes are now identified as CerS. Each CerS exhibits fatty acyl chain length specificity as well as differential tissue distribution. CerS1 is specific for stearic acid C18 and is expressed in brain, skeletal muscle, and testis. CerS2 is specific for C20â€”C26 fatty acids and is expressed in the liver and kidney. CerS3 is specific for C22â€”C26 fatty acids and is expressed in the skin and testis. CerS4 is specific for C18â€”C20 fatty acids and is ubiquitously expressed but with highest levels in liver, heart, skin, and leukocytes. CerS5 is specific for palmitic acid C16 and is ubiquitously expressed at low levels. CerS6 is specific for myristic C14 and palmitic acid and is expressed at low levels in all tissues. CerS1 is structurally and functionally distinct from the other five CerS all, of which contain a homeobox-like domain. The CERS1 gene is located on chromosome19p Transcription of the isoform 3 amino acids encoding mRNA begins from an alternative promoter than the other two mRNAs. The CERS2 gene is located on chromosome 1q The CERS3 gene is located on chromosome 15q The CERS4 gene is located on chromosome 19p The CERS5 gene is located on chromosome 12q The CERS6 gene is located on chromosome 2q The biological significance of ceramide synthesis and the activity of the CerS is demonstrated by studies in several different types of human cancers. In this regard CerS1 appears to most significant. Head and neck squamous cell carcinomas HNSCC exhibit a downregulation of Cceramide levels when compared to adjacent normal tissue. In the chemotherapy of certain cancers, CerS1 activity may also play a role. Enhanced expression of CerS1 has been shown to sensitize cells to a variety of chemotherapeutic drugs such as cisplatin, vincristine, and doxorubicin. The proposed mechanism for ceramide involvement in apoptotic processes involves the activation of the aspartate protease cathepsin D. Cathepsin D is associated with membranes and when activated by ceramides is released to the cytosol where it triggers the mitochondrial apoptosis pathway. Further evidence for the role of ceramides in negative growth responses is seen in cell cultures to which ceramide analogues are added. When derived from the sphingomyelins, ceramides are the products of the action of acid sphingomyelinase ASMase. The importance of sphingomyelin as a source of ceramide can be evidenced by the fact that the activation of the ASMase pathway is a shared response to the effects of cytokines, stress, radiation, chemotherapeutic drugs, and pathogenic and cytotoxic agents. The induction of ASMase, in response to apoptotic triggers, results in increased production of ceramides which then can initiate aspects of the apoptosis pathways as described above. In addition, there is ample evidence demonstrating that the accumulation of cellular ceramides is associated with the pathogenesis of diseases such as obesity , diabetes , atherosclerosis, and cardiomyopathy.

For example, studies in mice have correlated endogenous ceramides and glucosylceramides with the antagonism of insulin-stimulated glucose uptake and synthesis. An enhanced systemic inflammatory status as well as cellular stress have both been associated with insulin resistance. With respect to biological lipids, excess lipid intake, especially saturated fatty acids, leads to mitochondrial and endoplasmic reticulum ER stress. Increased fat oxidation in mitochondria leads to the production of reactive oxygen species ROS which are known to result in insulin resistance. Both mitochondrial and ER stress can result in apoptosis. Excess fatty acid intake also interferes with normal insulin receptor-mediated signal transduction resulting in insulin resistance. For more information on the role of fats and mitochondrial stress in insulin resistance visit the Insulin Functions page. Obesity , which results in insulin resistance and development of type 2 diabetes, has long been associated with low-grade systemic inflammation. The correlation between obesity, ceramide synthesis, and insulin resistance is discussed below. Experiments in cell culture, involving both adipocytes and skeletal muscle cells, have shown that ceramides inhibit insulin-stimulated glucose uptake by blocking translocation of GLUT4 to the plasma membrane as well as by interfering with glycogen synthesis. The phosphorylation leads to reduced affinity of the kinase for phosphoinositides. The role of saturated fatty acids in increased levels of ceramides has been demonstrated by adding palmitate to cultured muscle cells. An alternative means to examine the effects of ceramides on insulin sensitivity is to block the pathways of ceramide metabolism. Under conditions of ceramidase inhibition there is an exagerated effect of palmitic acid addition on insulin resistance. Conversely, if one overexpresses acid ceramidase, the inhibition of insulin signaling induced by palmitate addition is completely blocked. The cellular effects of glucosylceramide, although similar to ceramides themselves, does exhibit cell-type specificity. Glucosylceramide is the precursor for a complex family of gangliosides, for example the GM3 ganglioside. Adipocytes are highly sensitive to the inhibitory effects of glucosylated sphingolipids on insulin actions, whereas muscle cells are unaffected. The significance of the accumulation of these gangliosides has been demonstrated in mice lacking GM3 synthase which generates the major ganglioside precursor. These mice are protected from insulin resistance and glucose intolerance when fed a high-fat diet.

Chapter 3 : Design of Metabolism or How Biological Order Comes About

Metabolism and biological activities of inositol pentakisphosphate and inositol hexakisphosphate InsPe Fig. 2. Metabolism of inositol polyphosphates.

This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution license http: This article has been cited by other articles in PMC. Abstract Mangosteen Garcinia mangostana L. Numerous in vitro studies have shown that these xanthones possess anti-oxidant, anti-proliferative, pro-apoptotic, anti-inflammatory and anti-carcinogenic activities. This review will a critically address recent reports of in vivo studies on the bioavailability and metabolism of mangosteen xanthones, b update the in vitro and in vivo data on anti-cancer and anti-inflammatory activities of mangosteen xanthones, and c suggest needed areas of inquiry regarding the absorption, metabolism and efficacy of mangosteen xanthones. Introduction Juice blends and other products containing exotic fruits, also known as superfruits, have been aggressively marketed for their proposed health benefits. This has resulted in a steady rise in sales of superfruit juices and products to consumers interested in their personal health. Mangosteen is one such superfruit that is produced by Garcinia mangostana L. The genus Garcinia is native to Asia and Africa and includes more than distinct species from which several families of bioactive compounds such as xanthones, flavonoids, triterpenoids, and benzophenones have been isolated and characterized [1]. Although many Garcinia species including G. The mangosteen tree is mainly cultivated in Indonesia, Malaysia, the Philippines, and Thailand. Mature mangosteen trees range from 6 to 25 m. Production of the fruit generally requires 10 or more years with a yield of around fruits per tree that is increased in older trees. The pericarp of mangosteen fruit has been used in traditional medicine in Southeast Asia for centuries to treat infection, wounds, inflammation and diarrhea [3]. Products containing mangosteen juice or extract are a fast growing segment of the functional beverages market. Oftentimes, products marketed as mangosteen juice are a blend of numerous fruit juices with mangosteen being one of the less abundant components. Secondary metabolites, known as xanthones, have been isolated from the pericarp of mangosteen and are attributed to the medicinal properties of the fruit. Xanthones have a unique chemical structure composed of a tricyclic aromatic system C6â€”C3â€”C6. Isoprene, methoxyl and hydroxyl groups located at various locations on the A and B rings, resulting in a diverse array of xanthone compounds. Xanthones are found in a select few higher plant families. At least 68 distinct xanthones have been identified in different parts of the G. Details regarding the extraction and identification of these and other xanthones have been reviewed elsewhere [5].

Chapter 4 : The Metabolism of Baicalin in Rat and the Biological Activities of the Metabolites

The biological activities of omega-3 fatty acids (n-3 FAs) have been under extensive study for several decades. However, not much attention has been paid to differences of dietary forms, such as triglycerides (TGs) versus ethyl esters or phospholipids (PLs). New innovative marine raw materials, like.

 Pharmacological studies have demonstrated that THSG exhibits numerous biological functions in treating atherosclerosis, lipid metabolism, vascular and cardiac remodeling, vascular fibrosis, cardiac-cerebral ischemia, learning and memory disorders, neuroinflammation, Alzheimer and Parkinson diseases, diabetic complications, hair growth problems, and numerous other conditions. This review focuses on the biological effects of THSG in antiaging and antiaging-related disease treatments and discusses its molecular mechanisms. Introduction Aging is inevitable; it is a progressive, irreversible process that every human will experience in his life. The aging population of the international community brings increasing medical expenses and health care costs. There are many theory researches of aging mechanisms. The most famous one is the oxidative stress theory. Oxidative damage occurs in various aging-associated disease pathologies, especially the cardiovascular diseases and neurological diseases. Theoretically, antioxidant supplementation should be able to reduce the risk of aging-related diseases. The Mediterranean diet with red wine, fruits, vegetables, and other plant foods has been shown to have cardiovascular protection against oxidative damage. At present, the extraction of biological antioxidants from plants is becoming one of the hot topics in the field of medical chemistry. As early as A. The plant is processed to product radix Polygoni Multiflori preparata Figure 1 c , traditionally taken to increase vitality, improve the health of blood and blood vessels, blacken hair, strengthen bones, nourish the liver and kidney, and prolong life. Currently, Polygonum multiflorum Thunb. It is also used in many Chinese medicinal supplements to improve general health. THSG belongs to polyhydroxystilbene group. As a resveratrol analog with glucoside, THSG has been proved to possess strong antioxidant and free radical scavenging activities even much stronger than resveratrol in superoxide anion radical scavenging, hydroxyl radical scavenging, and DPPH radical scavenging [2]. Furthermore, 2-O-Glu group can stabilize the phenoxyl free radicals and they are easy to be hydrolyzed in extreme pH environments in the gastrointestinal environment. Contemporary pharmacological studies have demonstrated that THSG exhibits numerous biological functions in antiaging and antiaging-related disease treatments. In this review, we focus on THSG, discussing its biological effects and molecular mechanisms. Delaying the Senescence Effect A few years ago, we found that THSG can delay vascular senescence and markedly enhance blood flow in spontaneously hypertensive rats SHRs , but it does not affect blood pressure or body weight [4]. THSG promotes deacetylation of p53, a transcription factor associated with aging. Our unpublished data show that in vivo THSG is more effective in delaying vascular senescence than resveratrol. Furthermore, THSG upregulates klotho protein expression in cerebrum, heart, kidney, testis, and epididymis tissues of D-galactose induced aging mice [6]. THSG prolongs the mean, median, and maximum adult lifespans of C. THSG also exerts a higher antioxidative capacity in nematode compared with resveratrol and reduces the levels of the aging pigment lipofuscin. Atherosclerosis and Lipid Metabolism An experimental investigation using New Zealand rabbits demonstrated that THSG reduces atherosclerotic plaque accumulation caused by a high cholesterol diet, and lower plasma cholesterol, low-density lipoprotein LDL cholesterol, very-low-density lipoprotein VLDL cholesterol, and triglyceride levels [8]. THSG exhibited antioxidant properties and protected against apoptosis in a lysophosphatidylcholine- LPC- induced endothelial cell injury model [11]. Ten years ago, a Japanese group found that THSG does not affect the food intake, growth, or blood pressure of SHRs, consistent with our data [4 , 12], but significantly reduces free fatty acid content in serum. THSG significantly reduces cholesterol and neutral lipid content in the VLDL fraction and neutral lipid content in the

high-density lipoprotein HDL fraction in the blood, as well as neutral lipid content in the liver [12]. Another study reported that THSG administration to rats for 1 week can effectively control serum levels of total cholesterol and LDL cholesterol. The expression of LDL receptors in the liver was significantly upregulated in a high-fat-fed rat model [13]. Our recent study reported that orally administering THSG for 14 weeks significantly inhibited vascular remodeling and fibrosis in SHRs with increasing blood flow and with constant blood pressure [18]. Heart THSG improves cardiac ischemia-reperfusion, cardiac remodeling, and cardiac stem cells. The infarct size, ST segment recovery, and incidence of arrhythmia in the THSG postconditioning group are all significantly improved compared with the control group [19]. THSG has also been shown to promote mitochondrial biogenesis and induce the expression of erythropoietin EPO in nonhematopoietic cells, including primary cardiomyocytes, and enhance EPOâ€”EPO receptor autocrine activity. THSG robustly increases the endurance performance activity of healthy and doxorubicin-induced cardiomyopathic mice in ischemic disorders, stimulates myocardial mitochondrial biogenesis, and improves cardiac function [20]. In cardiac remodeling, THSG can attenuate pressure overload-induced cardiac pathological changes. THSG does not affect intracellular calcium ion dynamics at rest; however, in the ADP or thrombin stimulation, THSG reduces dose-dependently the rise in intracellular calcium flow [23]. Moreover, THSG promotes the differentiation of PC12 cells, increases the intracellular calcium level in hippocampal neurons, and facilitates high-frequency stimulation-induced hippocampal long-term potentiation LTP in a bell-shaped manner. Neuroinflammation Neuroinflammation is closely implicated in the pathogenesis of neurological diseases. Thus, the inhibition of microglial inflammation may have potential therapeutic significance for neurological diseases. Furthermore, in the pole test, THSG reduces the times required to turn the body and climbing down to the floor [36]. Cerebral Ischemia Previous studies have shown that THSG significantly decreases the percentage of apoptotic cells in injured rat brain tissue induced by ischemia reperfusion, promotes Bcl-2, and inhibits Bax protein expression in brain tissue [40]. THSG also promotes changes in animal nerve behavior; improves neurological function scores; increases the expression of NGF, growth-associated protein 43, and PKA catalytic subunit proteins; and presents a positive correlation between neurological function scores and determined protein expression [41]. Furthermore, the authors used an in vitro ischemic model of oxygen-glucose deprivation followed by reperfusion OGD-R , revealing that THSG reverses intracellular ROS generation and mitochondrial membrane potential dissipation and inhibits c-Jun N-terminal kinase JNK and Bcl-2 family-related apoptotic signaling pathway. Diabetes and Other Diseases 5. Diabetes The beneficial effects of THSG in alleviating diabetic complications are reflected in diabetic nephropathy and gastrointestinal disorders. Treatment with THSG reduces the increase in total cholesterol and triglyceride levels of diabetic rats [43]. For disorders of gastrointestinal function in diabetes, long-term preventive treatment with THSG relieves delayed gastric emptying and increases intestinal transit, impaired nonadrenergic-noncholinergic relaxations, and deficiency of neuronal NO synthase expression in streptozotocin-induced diabetic mice. Bone Mineral Density Recently, a study reported that THSG promotes bone mineral density and bone strength in the femoral bones of rats and enhances the bone mineral weight and bone mineral size in the iliac and humeral section after 90 days of administration [45]. In vitro, THSG also promoted hair growth in the cultured tentacles follicles of mice, with longer hair than that in the control group after 8 days [47]. Another report indicated that in vitro THSG increased the proliferation of dermal papilla cells of mice compared with the control group [48]. In addition, THSG promoted tyrosinase activity and melanin biosynthesis dose-dependently [49 , 50]. Summary Although THSG has been found to exhibit many medicinal properties, because no systematic study has investigated its regulatory mechanisms and proteomics or genomics data, its functional targets remain unclear. Nevertheless, we summed up the signal transduction pathways that are regulated by THSG, shown in Figure 2 , which presents multipathway multitarget characteristics that block and activate different signaling and gene expression. In all the animal experiments in this study, the rats and mice were the main models Table 1. However, the experiments involving the genetic model and the specific gene knockout model were used less. In most studies, THSG has been administered daily by oral gavage, but

in some cases it has been delivered by intraperitoneal injection. The pharmacologic activity of THSH in low concentration in cellular studies is summarized in this review Table 2. Dosages of THSG in vitro are normally between 0. Then the high concentration of THSG may play a role in toxicological effects instead of activation effects. Because of this, clinical value may be restricted. Summary of animal experiments of THSG. Summary of experiments of THSG in vitro. The signal transduction pathways regulated by THSG in the antiaging and aging-related diseases. THSG displays different activities in blocking and activating signaling and gene expression in vitro and in vivo. From the perspective of drug effects, THSG achieves favorable results in delaying senescence and in treating aging-related diseases, especially in the cardiovascular and nervous system. Some studies have shown that THSG may be more effective than resveratrol in delaying senescence. Nevertheless, more research is necessary to explain the mechanism of THSG.

Chapter 5 : Molecules | Topical Collection : Phytochemicals: Biosynthesis, Metabolism and Biological Activ

Starch is widely used in the food and beverage, paper and textile industries. Genetic engineering will allow optimization of starch conversion technologies both by creating novel enzymes/micro.

Article in Comparative biochemistry and physiology. The user has requested enhancement of the downloaded file. All in-text references underlined in blue are linked to publications on ResearchGate, letting you access and read them immediately. Comparative Biochemistry and Physiology Part C â€" Effect of C2 ceramide on the inositol phospholipid metabolism uptake of 32P, 3H-serine and 3H-palmitic acid and apoptosis-related morphological changes in Tetrahymena P. In the present experiments the influence of phospholipid turnover and apoptosis related morphologic signs by one of this metabolite, C2 ceramide was studied, and compared to the control, untreated cells, in the unicellular Tetrahymena. The incorporation of phospholipid head group components serine, phosphorus show a clear time-dependence; while the incorporation of fatty acid component palmitic acid is very fast: The amount of total incorporated 32P was also decreased, on the other hand the lover concentration C2 ceramide 10 mM elevated the synthesis of inositol phospholipids. The higher concentration of C2 ceramide 50 mM had inhibitory effect on the synthesis of each phospholipids examined. This means that in the presence of the C2 ceramide the synthesis, recovery and turnover of phospholipids, participating in signal transduction, are altered. However these observations were based the uptake of labeled phospholipid precursors, which gives information on the dynamics of the process, without using lipid mass measurements. C2 ceramide also caused the rounding off the cells, DNA degradation and nuclear condensation. These latter observations point to morphological signs of apoptosis. The results call attention to the role of sphingomyelin metabolites on signalization of unicellulars, to the cross-talk between the inositol phospholipids and sphingomyelin metabolites, and the role of these molecules in the apoptotic processes at a low evolutionary level. Introduction Tetrahymena, as it takes place in the higher eukaryotes [9]. Signaling networks that use glycerophospholipid The cytokine tumor necrosis factor a TNFa has metabolites as second messengers have been demon- multiple biological activities. Enzymes has been identified as e. Ceramides have been im- metabolites [12]. PII S 98 P. Time course of the incorporation of 3H-serine a and 3H-palmitic acid b into the phospholipids of Tetrahymena. The experiments were done four times with a representative experiment shown. Treatments with TNFa resulted spectacular alter- and inhibits the normal function of contractile vacuoles ations in the phospholipid metabolism in Tetrahymena: We focused in the present paper the incorporation of 32P into the phospholipids and on the effect of C2 ceramide, a cell permeable analog of inositol phospholipids decreased and the ceramide pro- naturally produced ceramide, as in our earlier work [20] duction increased. Moreover these treatments reduced after TNFa treatments also this compound was, pre- cell growth, altered the morphometric indexes, in- sumably, responsible for the above mentioned creased chromatin condensation [20]. Our data led to alterations. This conclusion is supported by the phenomena by using of cell permeable ceramide ana- fact that C2 ceramide disturbs the actin cytoskeleton logue N-acetyl-sphingosine C2 ceramide. The effect of C2 ceramide on the incorporation of 3H-palmitic acid into the phospholipids of Tetrahymena after 5 min a and 30 min b treatment. Lipid separation, analysis as described in Fig. Materials and methods Germany. Materials chemicals used were of analytical grade available from commercial sources. Before the experi- PA, PC, ceramide and tryptone were obtained from ments the cells were washed with fresh culture Sigma St. The effect of C2 ceramide on the incorporation of 3H-serine into the phospholipids of Tetrahymena. Time-course of the incorporation of 3H-palmitic acid 2. Time course of the incorporation of 32 P into the and 3H-serine into the phospholipids of Tetrahymena phospholipids of Tetrahymena Tetrahymena cultures were treated with: Samples of 5 ml were taken after 5, 10, 1, 5, 15, 30 and 60 min. The phospholipids were 30 and 60 min. The incubation was stopped by rapid separated according the method of Suchard et al. After centrifugation the lipid The phospholipid samples were analyzed on silica gel G content of the cell pellet was separated according to the TLC plates; solvent system: The lipids were sepa-

methanol: The individual lipids were identified by parallel run of Comparative data are given by the laser densitometric authentic standards. The data represent means of four independent experiments 9 S. To get absolute values from fragmentation of Tetrahymena incorporated radioactivity of phospholipids, after the radiographic exposure the spots were scraped into scin- Tetrahymena cultures were treated with 10 or 50 mM tillation vials and the activities were measured by liquid C2 ceramide for 60 min. Non treated cultures served as scintillation counter. After treatments the cells were lysed, and the DNA was extracted and submitted to agarose gel elec- 2. Effect of C2 ceramide on the incorporation of trophoresis as described in [28]. The samples were 3 electrophoresed at 40 V for 6 h through a 0. DNA bands were visualized phospholipids of Tetrahymena under UV light after staining with ethidium bromide. Non C2 ceramide treated cells served as controls. Samples were taken Tetrahymena cultures were treated 10 or 50 mM C2 after 5 and 30 min in case of 32P after 1, 5, 15, 30 and ceramide for 60 min. Non treated cells served as con- 60 min. The lipid extraction and analysis were done trols. The gently washed 2. Effect of C2 ceramide on the chromatin cells were applied onto microscopic slides and were condensation of Tetrahymena photographed in light microscope; magnification: The prints were scanned by Hewlett Packard Washed and in fresh culture medium resuspended HP-Scan Jet II scanner and the data obtained were Tetrahymena cultures were divided into three experi- analyzed by a computer programme Biomorph 1. Samples were taken after 10 and 60 min. Analysis of the 6iability of the cells Feulgen reaction for DNA was done [8]. The After each treatment the viability of the cells was colour intensity of Feulgen reaction transparence, q analyzed by trypan blue exclusion. In the further mea- was assessed with a Zeiss Amplival cytophotometer at surements only the unlabeled viable cell populations nm. The cytophotometer measures the light perme- were used. Statistical treatment of data transparence, thus the lower cytophotometric values mean higher condensations. Changes in comparative values were monitored by laser densitometric measurements of radiograms of TLC-separated phospholipids. It was remarkable that in case of 50 3. Results mM C2 ceramide the 32P labeling appeared only after 15 min incubation with radioactive phosphorus. The lower The incorporation of 3H-serine into the phospho- C2 ceramide concentration 10 mM caused in each lipids of Tetrahymena show time-dependence Fig. The incorporation of 3H-serine into the phospho- Likewise the nucleosomal degradation refers to the lipids was inhibited by both 10 and 50 mM C2 ceramide effect of C2 ceramide on the nuclear structure: Partly the the controls Fig. The effect of C2 ceramide on the transparence q of Feulgen reaction product chromatin condensation in the nuclei of Tetrahymena. The data represent the mean 9 S. The results of present experiments corroborate this premise. In our experiments the phospholipid metabolism has 4. Discussion been detected by the use of 3H-labeled serine and palmitic acid as well as 32P, giving information on the Tetrahymena has receptor, hormone, second messen- dynamics of the processes, without using lipid mass ger systems, which are working seemingly similar to measurements. The incorporation of palmitic acid into vertebrate ones [6,13]. Receptor activated cyclic-AMP the phospholipids of Tetrahymena is very fast, and its [7], cyclic-GMP [21], calmodulin-dependent guanylate intensity was not inhibited significantly by C2 ceramide cyclase [19], and inositol phospholipids [14] have very treatments. Whereas the incorporation of 32P and ser- important role in the regulation of the cellular functions ine, the components of phospholipid head groups, of Tetrahymena. The role of these sphingomyelin synthesis of glycerophospholipids and sphingolipids breakdown products are analogous to the role of glyc- alike. These metabolic steps take of some cellular functions as cell division, apoptosis, up a certain time, thus the time-dependence of serine etc. TNFa treatments generated ceramide also in this or- Treatments with C2 ceramide inhibit significantly the ganism [20], it was presumable that this sphingomyelin incorporation of serine into the most phospholipids, P. DAG from these these cells. These facts suggest a connection between phospholipids, and thus the common turnover of inosi- the inositol phospholipid turnover, C2 ceramide treat- tol phospholipids. The observations in the course of 32P incorporation The rounding off the cells in Tetrahymena is a sign of demonstrated similar phenomena. In case of 32P incor- prospective cell death. Moreover, as it is cleared by the poration the first radioactively labeled phospholipid is present experiments, after C2 ceramide treatment an- the PI; after that the PE contains the greatest part of

other apoptotic phenomena can develop. The C2 ceramide treatments retarded this condensation revealed by photometric measurements of labeling, but in case of lower concentration 10 mM at Feulgen reaction-product or the nucleosomal degrada- 15 min we measured higher labeled PI, PIP and PIP2 tion indicated by appearance of small â€" kB concentration, that in the controls. These findings indi- DNA fragments refer to apoptotic-like alterations: The rounding off the cells indicates also the portant role in signalization, it is presumable that the non-apoptotic cell death necrosis , however in the case inhibition of the normal function and the turnover of of necrosis Tetrahymena does not show an oligonu- this system lead to numerous signalization problems. The results of Phosphoinositides have been reported to be impor- trypan blue exclusion also strengthen our supposition tant in the regulation of actin polymerization [5]. After about the apoptotic phenomenon: Depolymerization of F-actin cells are genetically programmed to kill themselves, during the TNFa-induced apoptosis occurs after the only constant support from neighbouring cells keeps them alive [24]. Similar phenomenon is in the case of unicellulars [4]: Tetrahymena thermophila cells die rapidly when inoculated at low initial densities into chemically defined medium. Cell free, conditioned medium from high density cultures prevents cell death and activates proliferation [3]. Taken together, these results indicate that Tetrahymena cells produce and release growth factors which in appropriate concentra- tion stimulate the cells to survive and proliferate. These factors act in a variety of different ways which directly or indirectly activate second messenger pathways neces- sary to promote cell survival and proliferation [27]. It can be argued on the basis of our data presented here that C2 ceramide a inhibits the precise function of the signaling system e. Effect of C2 ceramide on the nucleosomal fragmentation of ramide inhibits the synthesis and release the growth Tetrahymena. DNA was extracted and electrophoresed in 0. DNA bands were visualized under UV can serve as an apoptosis mediating second messenger light after staining with ethidium bromide. The data represent averages 9S. A rapid method of total lipid extraction and purification. Can J Biochem Physiol ;

DOWNLOAD PDF METABOLISM BIOLOGICAL ACTIVITIES OF C(2)-CERAMIDE

Chapter 6 : www.nxgvision.com: Biochemistry: Metabolism

With respect to the intense in vivo formation of adenine and adenosine as products of cisZ and transZ metabolism in tobacco BY-2 cells and oat leaves (Figs 6, 7), degradation of [H]cisZ, [H]transZ, and [H]iP by CKX from crude extracts of two plant materials was determined.

A summary of metabolism The unity of life At the cellular level of organization, the main chemical processes of all living matter are similar, if not identical. This is true for animals , plants , fungi , or bacteria ; where variations occur such as, for example, in the secretion of antibodies by some molds , the variant processes are but variations on common themes. Thus, all living matter is made up of large molecules called proteins , which provide support and coordinated movement, as well as storage and transport of small molecules, and, as catalysts , enable chemical reactions to take place rapidly and specifically under mild temperature, relatively low concentration, and neutral conditions i. Moreover, those portions of protein molecules involved in performing similar functions in different organisms often comprise the same sequences of amino acids. There is the same unity among cells of all types in the manner in which living organisms preserve their individuality and transmit it to their offspring. For example, hereditary information is encoded in a specific sequence of bases that make up the DNA deoxyribonucleic acid molecule in the nucleus of each cell. Only four bases are used in synthesizing DNA: Just as the Morse Code consists of three simple signalsâ€”a dash, a dot, and a spaceâ€”the precise arrangement of which suffices to convey coded messages, so the precise arrangement of the bases in DNA contains and conveys the information for the synthesis and assembly of cell components. Some primitive life-forms, however, use RNA ribonucleic acid; a nucleic acid differing from DNA in containing the sugar ribose instead of the sugar deoxyribose and the base uracil instead of the base thymine in place of DNA as a primary carrier of genetic information. The replication of the genetic material in these organisms must, however, pass through a DNA phase. With minor exceptions, the genetic code used by all living organisms is the same. The chemical reactions that take place in living cells are similar as well. Green plants use the energy of sunlight to convert water H2O and carbon dioxide CO2 to carbohydrates sugars and starches , other organic carbon -containing compounds , and molecular oxygen O2. In effect, carbon dioxide accepts and bonds with hydrogen, forming carbohydrates Cn[H2O]n. Living organisms that require oxygen reverse this process: The process that removes hydrogen atoms containing electrons from the carbohydrates and passes them to the oxygen is an energy-yielding series of reactions. In plants, all but two of the steps in the process that converts carbon dioxide to carbohydrates are the same as those steps that synthesize sugars from simpler starting materials in animals, fungi, and bacteria. Similarly, the series of reactions that take a given starting material and synthesize certain molecules that will be used in other synthetic pathways are similar, or identical, among all cell types. From a metabolic point of view, the cellular processes that take place in a lion are only marginally different from those that take place in a dandelion. Biological energy exchanges The energy changes associated with physicochemical processes are the province of thermodynamics , a subdiscipline of physics. The first two laws of thermodynamics state, in essence, that energy can be neither created nor destroyed and that the effect of physical and chemical changes is to increase the disorder, or randomness i. Although it might be supposed that biological processesâ€”through which organisms grow in a highly ordered and complex manner, maintain order and complexity throughout their life, and pass on the instructions for order to succeeding generationsâ€”are in contravention of these laws, this is not so. Living organisms neither consume nor create energy: From the environment they absorb energy in a form useful to them; to the environment they return an equivalent amount of energy in a biologically less useful form. The useful energy, or free energy , may be defined as energy capable of doing work under isothermal conditions conditions in which no temperature differential exists ; free energy is associated with any chemical change. Energy less useful than free energy is returned to the environment, usually as heat. Heat cannot perform work in biological systems because all parts of cells have essentially the same temperature and

pressure. Page 1 of 7.